Hemolytic Uremic Syndrome (Postdiarrheal)

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1) THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Hemolytic uremic syndrome (HUS) is a syndrome characterized by anemia, renal injury and low platelet count. Among children, the most common cause of HUS is infection with a Shiga toxin-producing organism, most commonly *Escherichia coli* O157:H7 or some other strain of enterohemorrhagic *E. coli* (EHEC). *Shigella dysenteriae* also produces Shiga toxin, and infection with this organism can also cause HUS.

B. Clinical Description and Laboratory Diagnosis

HUS is an acute illness characterized by the sudden onset of thrombocytopenia and hemolysis with fragmented red blood cells, and acute anuric renal failure. For HUS caused by infection with a Shiga toxin-producing organism, the syndrome will usually manifest itself three to 10 days after the onset of a diarrheal illness, often including bloody diarrhea. Approximately 2–7% of cases of EHEC, such as *E. coli* O157:H7, develop HUS. Thrombotic thrombocytopenic purpura (TTP) is another potential consequence of infection with a Shiga toxin-producing organism. TTP is similar to HUS with more prominent neurologic signs. HUS is most commonly seen in children, whereas TTP is more commonly seen in adults. HUS in children can be fatal. Most cases of HUS, but few cases of TTP, follow an acute gastrointestinal illness (usually diarrhea).

Laboratory confirmation is based upon identifying evidence of anemia with microangiopathic changes: presence of fragmented red blood cells (schistocytes, burr or helmet cells) on peripheral blood smear, and acute renal failure: hematuria, proteinuria and/or elevated creatinine level

Since HUS and TTP have multiple causes, only HUS or TTP that follow an acute diarrheal illness should be reported.

C. Reservoirs

While cattle appear to be the most significant reservoir for *E. coli* O157:H7 and other EHEC strains, other animals, such as deer, are also known to carry these bacteria. In contrast, humans are the only known reservoir for *S. dysenteriae* type 1.

D. Modes of Transmission

See the chapters on *E. coli* O157:H7 and *Shigella* for modes of transmission for each organism.

E. Incubation Period

Onset of HUS usually occurs 3 to 10 days after the onset of diarrhea. Diarrhea may have resolved and the patient may appear to be improving when the onset of HUS occurs. For the incubation periods of the specific bacteria, refer to the chapters on *E. coli* O157:H7 and *Shigella.*

F. Period of Communicability or Infectious Period

People with HUS may be infectious if still shedding *E. coli* O157:H7 or *Shigella* in their stool. Refer to the chapters on each of these organisms for information on their infectious periods.

G. Epidemiology

HUS is seen worldwide and may occur in 5 to 10% of *E. coli* O157:H7 infections of children under 10 years of age. A bacterial pathogen is often not confirmed by a laboratory in cases of HUS, and therefore, the proportion

of cases of HUS due to specific bacterial infections is difficult to ascertain. Cases of HUS have been attributed to non-O157:H7 *E. coli* serotypes (*i.e.*, other EHEC strains), but the importance of these other serotypes in the occurrence of HUS is not known at this time. An average of 6 cases of HUS per year are reported to the NJDHSS.

2) REPORTING CRITERIA AND LABORATORY TESTING SERVICES

A. New Jersey Department of Health and Senior Services (NJDHSS) Case Definition

CASE CLASSIFICATION

A. CONFIRMED

A clinically compatible case and laboratory evidence of:

- Anemia (acute onset) with microangiopathic changes (schistocytes, burr cells, or helmet cells) on peripheral blood smear, **AND**
- Renal injury (acute onset) evidenced by either hematuria, proteinuria, and/or elevated creatinine level (i.e., >1.0 mg/dL in a child aged <13 years, or >1.5 mg/dL in a person aged >13 years, or >50% increase over baseline).

NOTE: A low platelet count can usually be detected early in the illness, but it may then become normal or even high**.**

B. PROBABLE

- An acute illness diagnosed as HUS or TTP that meets the laboratory criteria in a patient who does not have a clear history of acute bloody diarrhea in the preceding three weeks, **OR**
- An acute illness diagnosed as HUS or TTP that has began within three weeks of acute diarrhea **AND** meets the laboratory criteria except that microangiopathic changes are not conformed.

C. POSSIBLE

Initially reported on the basis of clinical diagnosis, until laboratory confirmation is obtained; no "possible" case classifications are retained.

NOTE: Some investigators consider HUS and TTP to be part of a continuum of disease. Therefore criteria for diagnosing TTP on the basis of CNS involvement and fever are not provided because patients diagnosed clinically as post diarrheal TTP also should meet the criteria for HUS. These cases are reported as post diarrheal HUS.

Note: See Section 3 C below for information on how to report a case.

B. Laboratory Testing Services Available

The NJDHSS and Environmental Laboratories (PHEL) will test stool specimens and culture isolates for the presence of Shiga toxin. **The PHEL requests that all laboratories submit within the three (3) days *all* isolates of *E. coli* 0157:H7 cultured for typing to aid in public health surveillance.** Specimens testing positive for this toxin will be tested for the presence of *E. coli* 0157:H7 and other *E. coli* strains that produce this toxin. If toxin producing organisms are isolated they will be referred to the Centers for Disease Control and Prevention (CDC) for further studies. For further information, contact the laboratory at 609.292.7368.

3) DISEASE REPORTING AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- HUS has been clearly demonstrated as important sequelae of infection with *E. coli* O157:H7. Because HUS cases generally come to medical attention, surveillance for HUS can serve as a marker for *E. coli* O157:H7 activity in the community and may lead to the identification of outbreaks at the state or local level. HUS is also an important event for assessing morbidity caused by *E. coli* O157:H7.
- To identify whether the case may be a source of infection for other persons (*e.g.*, a diapered child, daycare attendee or foodhandler) and, if so, to prevent further transmission.
- To identify transmission sources of public health concern (*e.g.*, a restaurant or a commercially contaminated food product) and to stop transmission from such sources.

B. Laboratory and Healthcare Provider Reporting Requirements

The New Jersey Administrative Code (N.J.A.C.) 8:57-1.8 stipulates that laboratories and healthcare providers report (by telephone, confidential fax, over the Internet using Communicable Disease Reporting System [CDRS] or in writing) all cases of HUS as defined by the reporting criteria in Section 2 A above to the local health officer having jurisdiction over the locality in which the patient lives. In addition laboratories should submit within the three (3) days *all* isolates of *E. coli* 0157:H7 cultured for typing to aid in public health surveillance.

C. Local Departments of Health Reporting and Follow-Up Responsibilities

1. **Reporting Requirements**

   The N.J.A.C. 8:57-1.8 stipulates that each local health officer must report the occurrence of any case of post diarrheal hemolytic uremic syndrome, as defined by the reporting criteria in Section 2 A above using the HUS Reporting form. A report should be filed electronically over the Internet using the CDRS or can be mailed or faxed to NJDHSS IZDP.

2. **Case Investigation**

   a. It is the health officer's responsibility to complete HUS Reporting form by interviewing the patient and others who may be able to provide pertinent information. When using electronic reporting, enter collected clinical information into the "Comments" section. Much of the information on the form can be obtained from the patient's healthcare provider or the medical record, and from the patient or his/her parent/guardian.

   b. Use the following guidelines for assistance in completing the form:
      1) Be sure to obtain as much information as possible about foods and activities during the week prior to onset of the diarrheal illness (not HUS onset). See also the chapters on *E. coli* O157:H7 and *Shigella* for more information on case follow-up.
      2) Accurately record the demographic/personal information.
      3) Complete the HUS Reporting form , including sections on HUS diagnosis, symptoms, laboratory findings, other medical information, and outcome.
      4) If there have been several attempts to obtain patient information (*e.g.*, the patient or healthcare provider does not return calls or respond to a letter, or the patient refuses to divulge information or is too ill to be interviewed), please fill out the form with as much information as possible. Please note on the form the reason why it could not be filled out completely. **If CDRS is used to report, enter the collected information into the "Comments" section.**

After completing the case report form, attach lab report(s) and mail in an envelope marked " Confidential" to the NJDHSS IZDP, or the report can be filed electronically over the Internet using the CDRS. The mailing address is:

NJDHSS
Division of Epidemiology, Environmental and Occupational Health
Infectious and Zoonotic Diseases Program
P.O.Box 369
Trenton, NJ 08625-0369

c. Institution of disease control measures is an integral part of case investigation. It is the local health officer's responsibility to understand, and, if necessary, to institute the control guidelines listed below in Section 4, "Controlling Further Spread."

4) CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (N.J.A.C 8:57-1.12)

Foodhandlers with HUS must be excluded from work, although people diagnosed with HUS are usually hospitalized and too ill to be working.

Note: A case of HUS is defined by the reporting criteria in Section 2 A of this chapter.

Minimum Period of Isolation of Patient

After symptoms have resolved, foodhandling facility employees may only return to work after producing **two (2)** negative stool specimens. If a patient has been treated with an antimicrobial, the stool specimen shall not be submitted until at least 48 hours after completion of therapy.

Note: Because the onset of symptoms of HUS usually occurs about a week after diarrheal illness, stool cultures frequently fail to identify a causative agent.

Minimum Period of Quarantine of Contacts

Contacts with diarrhea who are foodhandling facility employees shall be considered the same as a case-patient and handled in the same fashion. No restrictions otherwise.

Note: A foodhandler is any person directly preparing or handling food. This can include a patient care or child care provider.

B. Protection of Contacts of a Case

None.

C. Managing Special Situations

Daycare

A case of HUS in a daycare setting may be a marker for additional *E. coli* O157:H7 or *Shigella* infections within the facility. Surveillance for gastrointestinal illness should be heightened and children with GI symptoms should be referred to their healthcare providers for appropriate testing. If the patient has been diagnosed with *E. coli* O157:H7 or *Shigella*, please refer to the appropriate chapter of this manual for that disease. Contact the NJDHSS IZDP at 609.588.7500 for assistance in managing the follow-up of a case of HUS in a daycare setting.

School

A case of HUS in a school setting may be a marker for additional infections with *E. coli* O157:H7 or *Shigella* within the school, especially among classes with younger children. Surveillance for gastrointestinal illness should be heightened and students with GI symptoms should be referred to their healthcare providers for appropriate testing. If the case has been diagnosed with *E. coli* O157:H7 or *Shigella* please refer to the appropriate section of this manual for that disease. Contact the IZDP at 609.588.7500 for assistance in managing the follow-up of a case of HUS in a school setting.

Reported Incidence Is Higher than Usual/Outbreak Suspected

If the number of reported cases of HUS in a city/town is higher than usual, or if an outbreak is suspected, investigate to determine the source of infection and mode of transmission. A common vehicle (such as water, food or association with a daycare center) should be sought and applicable preventive or control measures should be instituted. Control of person-to-person transmission requires special emphasis on personal cleanliness and sanitary disposal of feces. Consult with the NJDHSS IZDP at 609.588.7500. IZDP staff can help determine a course of action to prevent further cases and can perform surveillance for cases that may cross several jurisdictions and therefore be difficult to identify at a local level.

D. Preventive Measures

Environmental Measures

Implicated food items must be removed from the environment. A decision about testing implicated food items can be made in consultation with the IZDP and the Food and Drug Safety Program (FDSP). FDSP can help coordinate pickup and testing of food samples. If a commercial product is suspected, FDSP will coordinate follow-up with relevant outside agencies (e.g., FDA, USDA). FDSP is reachable at 609.588.3123.

Note: The role of the FDSP is to provide policy and technical assistance with the environmental investigation such as interpreting the New Jersey Food Code, conducting a hazardous analysis and critical control points (HACCP) risk assessment, initiating enforcement actions and collecting food samples.

Personal Preventive Measures/Education

To avoid future exposure, advise individuals to:

- Wash their hands thoroughly with soap and water before eating or preparing food, after using the toilet and after changing diapers.
- After changing diapers, wash the child's hands as well as their own.
- Dispose of feces in a sanitary manner, especially in daycare centers or other institutional settings.
- Scrub their hands thoroughly after assisting in the following: caring for someone with diarrhea, cleaning toilets, and changing soiled diapers, clothing or bed linens.
- Send back all undercooked hamburger for further cooking.
- Cook all ground beef and hamburger thoroughly.
- Drink only pasteurized milk, juice, or cider.
- Wash fruits and vegetables thoroughly, especially those that will not be cooked.

ADDITIONAL INFORMATION

A *Hemolytic Uremic Syndrome Fact Sheet* can be obtained at the NJDHSS website at <http://www.state.nj.us/health>. Click on the "Topics A to Z" link and scroll down to the subject *Hemolytic Uremic Syndrome*

The CDC surveillance case definition for hemolytic uremic syndrome is the same as the criteria outlined in Section 2A of this chapter. CDC case definitions are used by state health departments and CDC to maintain uniform standards for national reporting. For reporting to the NJDHSS, always refer to the criteria in Section 2 A.

REFERENCES

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